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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WEGERT, SANDRA L	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 08/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/024,535	MARCEL ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *3-14,16-19,21 and 23-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,15,20 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 May 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

The arguments and Declaration under 37 CFR §1.132, submitted 2 June 2005, have been entered. Claims 1-50 are pending. Claims 3-14, 16-19, 21 and 23-50 are withdrawn. Claims 1, 2, 15, 20 and 22 are under examination as well as the following secondary Inventions: SEQ ID NO: 2 and *impaired social activity linked to sexuality*.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections and/or Rejections

Informalities- Continuity

The objection to the Specification, for failing to comply with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120, is *withdrawn*. Applicant inserted a reference to the prior application in the first sentence of the specification (Response, 2 June 2005).

Oath

The objection to the oath/declaration, for not identifying prior applications, is *withdrawn*. Applicant submitted a newly-executed oath/declaration listing the applications upon which

priority is relied for the instant application. See below for objections to the newly-executed oath/declaration.

Claim Rejections

The rejection of Claim 1 under 35 USC § 112, second paragraph-Indefiniteness, for recitation of *peptidomimetic,* is *withdrawn.* Applicants amended Claim 1 so that it no longer recites use of a *peptidomimetic* of SMR1 peptide (2 June 2005).

The rejection of Claim 1 under 35 USC § 112, first paragraph-Enablement, for recitation of *peptidomimetic,* is *withdrawn.* Applicants amended Claim 1 so that it no longer recites use of a *peptidomimetic* of SMR1 peptide (2 June 2005). See below for maintained rejections under 35 USC § 112, first paragraph-Enablement.

The rejection of Claim 1 under 35 USC § 112, first paragraph-Written Description, for recitation of *peptidomimetic,* is *withdrawn.* Applicants amended Claim 1 so that it no longer recites *peptidomimetic* (2 June 2005). See below for maintained rejections under 35 USC § 112, first paragraph-Written Description.

Maintained/New Objections and/or Rejections

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because:

Non-initialed and non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

A properly executed oath or declaration which complies with 37 CFR 1.67(a) and identifies the application by application number and filing date is required.

Claim Objections -

The objection to Claim 2 because it recites non-elected inventions, as set forth at page 4 of the previous Office Action (2 December 2004), is *maintained.* Applicants have argued that the other recited peptides in Claim 2 are related as species. However, the other recited SEQ ID NO's were properly restricted as distinct *inventions* having different functions in the organism. It would therefore constitute an undue burden to examine all the gene products recited, and associate each of them with a disorder. The restriction requirement was made final in the previous office Action (2 December 2004).

Appropriate correction is required.

Claim Rejections- 35 USC § 112, second paragraph

The rejection of Claims 1 and 15 for reciting indefinite claim language is *maintained.* One skilled in the art cannot determine the metes and bounds of the claimed invention because it is not clear what the phrases mean: "impaired social activity" and activity "linked to sexuality." Both "impaired social activity" and activity "linked to sexuality" are poorly defined in the art, and their relationship to each other in the claims is indefinite. Furthermore, "impaired social activity linked to sexuality" disorders are poorly defined in the Specification or appear to encompass many genera of diseases and disorders, including physiological (pages 14-17). Applicants have argued (page 13, 2 June 2005) that "one skilled in the psychiatric or

psychological arts would readily understand" what is meant by the disorders encompassed by the claims. However, the disorders must be named using language that is typical of one skilled in the psychiatric arts, so that it can be determined exactly which treatments are being claimed.

Claim Rejections- 35 USC § 112, first paragraph-Enablement

Claims 1, 2, 15, 20 and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification is not enabling for a method of administering the SMR1 peptide of SEQ ID NO: 2 in order to treat a mental disorder such as *impaired social activity linked to sexuality*. The reasons for this rejection were given in the previous Office Action (pages 5-8, 2 December 2004).

Claims 1, 2, 15, 20 and 22 are drawn to a method of treating a mental disorder, specifically *impaired social activity linked to sexuality,* by administering the short peptide of SEQ ID NO: 2 to mammals. Dependent claims recite a mental disorder which *comprises symptoms of more that one mental disorder* and routes of administration of the peptide.

Experiments were described in the specification in which FG-005 peptide (also called SMR1, QHNPR, and SEQ ID NO: 2) was administered intravenously, at doses of 3-30μg/kg, to normal male rats. Data were collected on the general alertness, anxiety levels and insensitivity to pain of the treated animals. The most comprehensive data reported the frequency and duration of several sexual behaviors when peptide-treated male rats were presented with female rats. Treated rats slept less, were reluctant to mount a female rat initially- but had more episodes of

sex subsequently- and spent more time grooming both himself and his cage-mate (see Tables I-III, instant Specification).

A sufficient amount of direction or guidance is lacking in claims 1, 2, 15, 20 and 22. The specification describes the intravenous administration of SEQ ID NO: 2 and the measurement of the duration and frequency of several rat sexual behaviors. However, nowhere in the specification is a method described that is a treatment of *impaired social activity linked to sexuality,* as applied to humans or other mammals, including rats. Nowhere in the instant Disclosure is a nexus described between the behaviors caused by SEQ ID NO: 2, and a well-defined disorder in human beings. Nor does current or prior literature suggest actual disorders that might be treated with the peptide of SEQ ID NO: 2 (Rougeot, et al, 1998, Biomed. Rev., 9: 17-32). And there were no animal models presented in the instant Specification that suggest such disorders. Furthermore, there was no discussion, or definition given, concerning the relationship between impaired social activity and sexuality in such disorders. While it was shown that injected male rats groomed more and had more sex when presented with a female rat, it is not clear which human condition the untreated group was meant to model. Nor is it known which disorder the method is meant to treat. The Specification defines the disorder as such:

"In certain preferred embodiments, the DSM-III disorder is impaired social activity linked to sexuality. As used herein, 'impaired social activity linked to sexuality' is impairment of social relationship to a sexual partner, which can lead to impairment of occupational functioning" (Specification, paragraph 54).

In fact, the Diagnostic and Statistical Manual of Mental Disorders lists no such disorder.

The psychiatric disorders that appear most-similar to "impaired social activity linked to

sexuality," as discussed in the instant Specification, are perhaps the genus of Hypoactive Sexual Desire Disorders (American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition. Washington, DC, American Psychiatric Association, 1994, section 302.71, pages 496-497). These human disorders are characterized by a decreased sexual interest that is not due to physiological factors. There is no discussion in the DSM-IV of "impaired social activity" in the context of disorders of sexual interest. Applicants also refer to a website describing "sexual, gender identity disorders" as "disturbances in sexual desire that cause a marked level of distress and interpersonal difficulties" (page 13, Response of 2 June 2005). However, no website was given or could be located that described "sexual, gender identity disorders" in such a way, or described the use of normal male rats to model such a disorder. The Diagnostic and Statistical Manual of Mental Disorders chapter on Sexual and Gender Identity Disorders lists 20-30 disorders and subtypes. While it is true that "one skilled in the psychiatric or psychological arts would readily understand" (page 13, Response) what is meant by the disorders encompassed by the claims, they still must be named, as well as well-defined. The examiner cannot determine what disorder is being treated, but it is probably not well-modeled by normal rats, especially considering that all "Sexual and Gender Identity Disorders," as defined in the DSM-IV, are characterized by marked distress and disruption (*Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition. Washington, DC, American Psychiatric Association, 1994, section 302.71).

Likewise, the Declaration submitted under 37 CFR § 1.132 is insufficient to overcome either the Enablement or Written Description rejections made under 35 USC § 112, first

paragraph (note: the Declaration seems to discuss only the Written Description rejection, but uses references important in the determination of Enablement). In the Declaration, the parasitologist Dr. Renoncet-Ungeheuer discusses several physiological and behavioral human conditions that are well-modeled in rats, including drug abuse, schizophrenia, epilepsy and the association between sex steroids and normal sexual behavior in male and female rats (note: the examiner could not locate some of the references referred to in the Declaration, and they have not been submitted with the Response). It is not surprising that many physiological and behavioral human conditions can be modeled in animals: mammals, in particular, have many cellular processes, neurotransmitters, hormones, receptors, enzymes and brain pathways that are similar to those of human beings. Dr. Renoncet-Ungeheuer gives several good examples where there is a direct correlation. For example, castration of both male rats and male humans results in a sharp drop in libido/sexual interest (Cormio, et al, 2005, International Journal of Impotence Research, 17: 23-26). Thus, castrated male rats are good models for several conditions in the human male characterized by low/absent androgens. In all examples discussed by Dr. Renoncet-Ungeheuer, with the exception of erectile dysfunction, the animals used as a model were *not normal*. They were made dependent on drugs, or they were stressed in some dramatic way, or they were born with a genetic defect, or they were castrated, all in order to closely mirror a human condition. This differs from the instant Application in which normal rats were used to model a human condition of abnormal sexual behavior. The Newport, et al paper, discussed by Dr. Renoncet-Ungeheuer (2002, Am. J. Psychiatry, 159(8): 1265-1283), describes some characteristics of good animal models of human behavioral disorders, the most important probably being their accuracy: "the validity of an animal model is contingent on [ ] its accuracy

in portraying the phenomenology and treatment response of a corresponding human illness" (page 1266, 7th paragraph). They also caution against using analogous animal behaviors as models, when homologous behaviors are more appropriate. For example, a bird species that kills its young during a food shortage is not a good model of child abuse in humans, because the two behaviors are only analogous behaviors that lack similar underlying determinants. In other words, its the lack of similar underlying determinants of a behavior that makes an animal model of human behavior less-than-useful. The Newport, et al paper does not discuss using normal animals to model human diseases, presumably because it is not often done. The paper advises the most caution when discussing the use of animal models of psychiatric diseases (page 1267, second paragraph), stating: "Because the pathophysiology of mental disorders remains obscure, the homology of an animal model to a human psychiatric condition cannot be absolutely demonstrated." It can be assumed, then, that a normal animal is a very poor model of a human behavioral condition, since it has no underlying pathophysiological determinants whatsoever.

For the reasons discussed above, treatment of a mental disorder by administration of SEQ ID NO: 2 is not enabled by the instant Disclosure.

Furthermore, Applicants are not enabled for the routes of administration specified in Claim 22. The Specification is enabling only for acute venous peripheral administration of the peptide. Applicants have argued that it "would be well within the skill of those in the medical or pharmaceutical arts to select other routes of administration" (page 15, Response). Applicants cite Pettit and Gombotz, (1998, TIBTECH, 16: 343-349 column 6), as evidence that peptides may be administered orally. However, that section of the paper discusses the theoretical use of

polyanhydride microspheres. Had the applicant performed the experiments using orally-administered microspheres comprising SEQ ID NO: 2, this particular route of administration would then be enabled. However, claimed methods, particularly treatment methods, must be worked out more-or-less completely at the time of filing of a patent application. Claiming routes of administration that have been shown to be largely ineffective with peptides, and then not describing sufficient details- such as doses, solvents, carriers, etc- indicates that significant experimentation must be undertaken to enable these methods. Routes of administration can have a dramatic effect on drug disposition, and on peptide disposition in particular (Pettit and Gombotz, 1998, TIBTECH, 16: 343-349, Table 1, for example). As suggested above, peptides are almost certainly *digested* when administered orally. Likewise, proteases abound in many tissues. These examples and others illustrate that the route of administration disclosed in the instant Specification does not reasonably predict untested routes of administration.

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation required to determine how to administer the SMR1 peptide to treat a sexual disorder, the lack of direction or guidance in the specification regarding the same, the lack of working examples that associate a sexual disorder in humans with normal rats, the state of the art which acknowledges the complexity of behavioral disorders, and the breadth of the claims which embrace methods of using the peptide to treat human conditions, and untested methods of administration -undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

35 USC § 112, first paragraph-Written Description

Claims 1, 2, 15, 20 and 22 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The reasons for this rejection were given in the previous Office Action (pages 8-10, 2 December 2004).

Claims 1, 2, 15, 20 and 22 are directed to methods of treating a mental disorder by administering an SMR1 peptide. Further, the claims recite treatment of impaired social activity linked to sexuality, disorders that comprise symptoms of more than one disorder, and alternative routes of administration of the polypeptide.

The specification teaches administration of a polypeptide (SEQ ID NO: 2) to normal male rats. However, the specification does not teach treatment of a mental disorder in humans, and does not disclose an animal model of a mental disorder in the current Specification. The description of experiments in which SEQ ID NO: 2 is injected into normal rats is not adequate written description of a genus of treatment methods that can be applied to humans.

Applicants have argued that "there can be no issue of whether or not this subject matter is described by the disclosure" (page 15, response). However, Written Description is not an issue of description of the claimed method, but rather one of *possession*. Adequate written description requires more than a mere statement that a method is part of the invention: the actual treatment itself is required. Applicants are not in possession of a method of treating any mental disorder or any sexual behavioral disorder in humans or animals and were not in possession of routes of administration of the disclosed peptide other than venous.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Brenda Brumback, can be reached at (571) 272-0961.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SLW
14 August 2005

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER